REMARKS

I. INTRODUCTION

In response to the Office Action dated September 9, 2004, claims 21 and 22 have been amended. Claims 21-27 and 32-39 remain in the application. Entry of these amendments, and reconsideration of the application, as amended, is requested.

II. AMENDMENTS

Applicants have amended the Sequence Listing to explicitly note that C-5 methylcytosines indicated in the oligonucleotides GC-Box bMET, GC-Box pMET, GC-Box cMET, GC-Box dMET, GC-Box eMET, and CRE aMET listed in Figure 1B are, in fact methylcytosines. Submitted herewith is a Statement indicating that this corrected Sequence Listing does not introduce new matter, and that the content of the paper and computer readable forms submitted herewith is the same.

Applicants have amended the claims as indicated above. These amendments were made solely for the purpose of clarifying the invention, and do not introduce new matter or raise new issues. Claims 21 and 22 have been amended to clarify that the enzyme/ synthetic inhibitor molecule complex recited in the claims contacts the DNA whose methylation is inhibited by the claimed method. This amendment is supported by the specification as originally filed, e.g., at page 6, lines 29-30.

Entry of these amendments is respectfully requested.

III. WRITTEN DESCRIPTION REJECTION

At page 2 of the Office Action, claims 36-39 were rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. The rejection is based on the recitation of SEQ ID NO: 10, 13, 14 and 15 in claims 36-39. These sequences are indicated in Figure 1B to include methylcytosine, but the corresponding SEQ ID NOs in the Sequence Listing do not explicitly identify the methylcytosine. Applicants respectfully disagree with the assertion at page 3 of the Office Action that the examiner does not believe applicants were in possession of all of the sequences as filed in the sequence listings. Applicants were clearly in possession of these sequences, with and without the methylcytosine. The examiner is correct,

however, in his belief that applicants intend the methylcytosine to be included in these SEQ ID NOs of the Sequence Listing.

In response, Applicants have amended the Sequence Listing to explicitly recite the methylcytosine. Accordingly, it is respectfully requested that the written description rejection be withdrawn.

IV. PRIOR ART REJECTIONS

At page 3 of the Office Action, the previous rejections under 35 U.S.C. §102(e) based on the Sufrin reference were withdrawn. At pages 3-8 of the Office Action, claims 21-27 and 32-35 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Sufrin. The rejection is based on an assertion that, although Sufrin teaches neither practicing their method in the presence of DNA nor the binding to an allosteric site on the DCMTase, it would have been prima facie obvious to one of ordinary skill in the art to practice the invention of Sufrin in the presence of DNA and the binding to an allosteric site would be inherently taught by Sufrin.

Because both of these assertions are in error, Applicants respectfully traverse these rejections.

Applicants' claims require (a) inhibiting methylation of DNA comprising (b) contacting DCMTase with a synthetic inhibitor molecule (c) so as to form an enzyme/synthetic inhibitor molecule complex that contacts DNA wherein (d) the inhibitor molecule comprises a C-5 methylcytosine molecule which (e) binds to an allosteric site on the DCMTase, which inhibits methyltransferase activity. The Patent Office has not shown that all of these elements are met by the cited reference. Sufrin fails to teach (a) inhibition (as it is understood by those skilled in the art), (c) formation of an enzyme/synthetic inhibitor complex that contacts DNA, or (e) binding to an allosteric site on the DCMTase.

With regard to the Examiner's assertion that the binding to an allosteric site would be inherently taught by Sufrin, the Examiner is respectfully reminded that inherency is relevant to anticipation, but not to a determination of obviousness. *Jones v. Hardy,* 230 USPQ 1021, 1025 (Fed. Cir. 1984). Even if the rejection were based on anticipation, the unwitting and unappreciated binding of the substrate to an allosteric site on the enzyme would not constitute anticipation of Applicants' claimed method. If a claimed method comprises steps identical to those of a method practiced in the prior art, and the same result would have been achieved in the prior art method, the

accidental or unwitting achievement of that result cannot constitute anticipation. *In re Marshall,* 578 F.2d 301, 198 USPQ 344 (CCPA 1978).

In addition to not teaching inhibition via binding to an allosteric site, the prior art does not teach or suggest contacting the DCMTase enzyme with the synthetic inhibitor molecule in the presence of DNA, or that the enzyme/inhibitor complex contacts DNA. Instead, Sufrin teaches **substrates** for the enzyme and compares the inherent activity of the different substrates. (See col. 4, lines 13-25, identifying the disclosed analogs as substrates that have the potential to be methylated by DNA methyltransferases.) Their "inhibition" is merely comparatively less activity when comparing one substrate to another, which is not what one skilled in the art would regard as inhibition. Moreoever, this observation of reduced activity with some substrates is not the same as using an inhibitor molecule to inhibit the ability of the enzyme to methylate a (separate) DNA molecule.

To the extent Sufrin suggests that their oligonucleotides inhibit DNA methyltransferase, Sufrin teaches this activity for oligonucleotides that contain 5-fluoro-cytosine (abbreviated as 5FC or FC), which were already known to interfere with DCMTase function and lead to cytological dysfunction (see Applicants' specification at page 2, lines 9-11) via action at a catalytic site, and not an allosteric site. Consistent with this point, Sufrin discusses oligonucleotides that contain methylcytosine as substrates, not inhibitors (see Sufrin at column 3, line 12, and column 5, lines 19-26 and 39-42).

The Examiner cites column 3, lines 28-33, of Sufrin as disclosing that their analogs are useful to inhibit DNA methyltransferase activity, and column 1, lines 42-53, discloses that their analogs are effective in inhibiting DCMTase activity in humans. The disclosure attributed to these citations is not present in the cited portions (or elsewhere) in Sufrin. Column 3, lines 28-33, refers to "the DNA analogs of the invention", which requires reference to the two preceding paragraphs. At lines 12 and 19 of column 3, Sufrin recites 5FC as a feature of some of their analogs. At column 5, lines 39-42, Sufrin makes it clear that the potent inhibitors they disclose are made by substituting FC for C in CG sequences – a mode of inhibition that does not involve binding to an allosteric site on the enzyme. The cited portion of column 1, lines 42-53, does not discuss inhibition by the analogs of Sufrin as asserted by the Examiner. Rather, this paragraph provides merely a general discussion of the known role that cytosine methylation plays in regulation of gene expression and how disruption of this regulation appears to be common in cancers.

The discussion in the Office Action that it would have been obvious to practice the method of Sufrin in the presence of DNA overlooks the fact that Sufrin does not teach all of the remaining elements of Applicants' claimed method. The ability to inhibit methyltransferase activity via an allosteric site and without having to use 5FC offers advantages over the prior art. Because Sufrin fails to teach each element of Applicants' claimed method, Sufrin does not anticipate or render obvious the invention and the rejection based on the prior art should be withdrawn.

V. CONCLUSION

In view of the above, it is submitted that this application is now in good order for allowance and such allowance is respectfully solicited. Should the Examiner believe minor matters still remain that can be resolved in a telephone interview, the Examiner is urged to call Applicants' undersigned attorney.

Respectfully submitted,

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